

## **REMARKS**

Applicants respectfully request reconsideration of the present case in view of the above amendments and the following remarks.

Claims 2, 3, 6-9 and 12 are currently pending. Claim 12 has been amended. No new matter has been inserted. Support for the amendment of claim 12 can be found in the specification at least at page 2, lines 3-5.

### **35 U.S.C. § 103**

Claims 2, 3, 6-9 and 12 remained rejected under 35 U.S.C. § 103(a) over SmithKline Beecham Corporation (WO 95/21944) in view of Høifødt et al. (WO 95/24648). Applicants respectfully traverse this rejection.

Claim 12 is directed to a “method for identifying genes differentially expressed between cells isolated from different tissues from the same individual.” Claim 12 requires the step of “detecting target cells from a first and a second tissue, wherein said first and said second tissues are from the same individual.” Neither SmithKline Beecham (WO 95/21944), nor Høifødt et al. (WO 95/24648) teach or suggest this feature. Therefore applicants respectfully submit that the combination of SmithKline Beecham and Høifødt fails to render claim 12 obvious.

Applicant's invention represents a comparison of gene expression patterns of the same type of cells (with the same origin=the primary tumor) found in different tissues, to which the cancer cells have metastasized. By using the tumor cell enrichment procedure Applicant's invention utilizes relatively pure populations of target cells, completely different from what SmithKline teaches, thereby avoiding the problems of SmithKline.

In sharp contrast to the teaching of Høifødt, Applicant's method compares gene expression profiles in tumor cells enriched from different sites/tissues in the same individual. At the time of the invention it was believed that the cells in cancer metastases in such different tissues expressed the same genes as found in the primary tumor, and that when tumor cells did metastasize the metastatic cancer cells would have identical gene

expression patterns, irrespective of their site of growth. The Applicant did not agree with that assumption, and the present method thus represents a contradiction of the accepted thinking of the prior art at the time. The present invention surprisingly made it possible to explore this issue by studying gene expression in pure cell populations, not facing the problem wherein various types of normal cells contaminate and confuse the expression pattern and signal intensity. Moreover, because the Applicant compares cells from different sites in the same individual it is now possible to avoid problems related to differences in gene expression in tumors from different individuals, not related to the ability of cancer cells to metastasize.

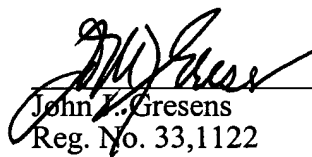
For at least these reasons, Applicants respectfully assert that the invention of claim 12 is not rendered obvious by the combination of SmithKline Beecham (WO 95/21944), nor Høifødt et al. (WO 95/24648). As claims 2, 3, and 6-9 are dependent on claim 12, they are also not rendered obvious. Applicants respectfully request that this rejection be withdrawn.

### Summary

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

9/15/04  
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